

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date
22 January 2004 (22.01.2004)

PCT

(10) International Publication Number
WO 2004/008103 A2

(51) International Patent Classification⁷: G01N (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, IIR, IIU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, I.K, I.R, I.S, I.T, I.U, I.V, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PII, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(21) International Application Number: PCT/US2003/022165

(22) International Filing Date: 14 July 2003 (14.07.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 60/395,272 12 July 2002 (12.07.2002) US

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(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, I.U, MC, NI, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MUTATIONS OF VOLTAGE-GATED ION CHANNELS THAT ALLOW THEM TO EXPRESS A VOLTAGE-INDEPENDENT PHENOTYPE AND AN IMPROVED METHOD TO USE THE SAME

Alignment of Voltage-Gated Potassium Channels Relevant Regions

hKv1.1 PYYITITGTRIAFQ----- FGNQKGEQATSLATLWRVTRI.VRVRTRI.FKLSRHSKG
mKv1.2 PYYITITGTRIAEKP----- EDAQOQGQANSLAI.LWRVTRI.VRVRTRI.FKLSRHSKG
Kv1.4 PYYITITGTRIAEQQG----- RENQGQQQANS.PATLWRVTRI.VRVRTRI.FKLSRHSKG
Kv1.3 PYYITITGTRIAEQR----- GNSQGQANSLAI.LWRVTRI.VRVRTRI.FKLSRHSKG
hKv1.5 PYYITITGTRIAECQVCC----- GGGGGQGQANSLAI.LWRVTRI.VRVRTRI.FKLSRHSKG
ShakerB PYYITITLATTVAEEDDTLN.LPKAFAVSPCDNSNQANSLAI.LWRVTRI.VRVRTRI.FKLSRHSKG
zKv3.1 PYYITITLVC----- LSCLSLSSKAQWVLCFLRVFRVFRVILRLFLTRBPFV
zKv2.1 PYYVITITFLTEGJKS----- VLRQFQNVFRVVAQITRIMRII.RLKLARHSTG
hKv4.2 PYYIGLVMTDNEODVS----- GAFVYI.RVFRVFRVPRIFAFS?RHSQG

hKv1.1 LCTLQTLKASMRELGLLIFPFLFGVTLI.PGAVYFAFAE----- FAFGQHPSGT?PDA
mKv1.2 LCTLQTLKASMRELGLLIFPFLFGVTLI.PGAVYFAFAE----- ERDSCOPPSIPDA
Kv1.4 LQIQLQTLKASMRELGLLIFPFLFGVTLI.PGAVYFAFAE----- EYTHFQSIQDA
Kv1.3 LQIQLQTLKASMRELGLLIFPFLFGVTLI.PGAVYFAFAE----- DFTSGFSSIPDA
hKv1.5 LQIQLQTLKASMRELGLLIFPFLFGVTLI.PGAVYFAFAE----- NOOTHFSISIDDA
ShakerB IGTIGRTTAK3MREI.RLITFFLFGVTLI.PGAVYFAFAE----- SENSFPKSIPDA
zKv3.1 LWRVLTGHTLRASTHETLLLII.FIALG/LI.PATMIIYAYRIGAQPNDPSASEETHPRKNIPIG
zKv2.1 LQSLGCPFLRSTHETELGLLII.LI.PATMIIYAYRIGAQPNDPSASEETHPRKNIPIG
hKv4.2 LRLIGGYFLKSCASELGFLLFSLTMAIIIFATVMYEAEG----- EDDTKRKSIPDA
hKv1.1 FWWAVVSMTTVGYGDMYPVTTIGGRIVGS.LCAIAGVLTIALEP.PVIVSN.FNYFYBRETEGE
mKv1.2 FWWAVVSMTTVGYGDMYPVTTIGGRIVGS.LCAIAGVLTIALEP.PVIVSN.FNYFYBRETEGE
Kv1.4 FWWAVVSMTTVGYGDMYPVTTIGGRIVGS.LCAIAGVLTIALEP.PVIVSN.FNYFYBRETEGE
Kv1.3 FWWAVVSMTTVGYGDMYPVTTIGGRIVGS.LCAIAGVLTIALEP.PVIVSN.FNYFYBRETEGE
hKv1.5 FWWAVVSMTTVGYGDMYPVTTIGGRIVGS.LCAIAGVLTIALEP.PVIVSN.FNYFYBRETEGE
ShakerB FWWAVVSMTTVGYGDMYPVTTIGGRIVGS.LCAIAGVLTIALEP.PVIVSN.FNYFYBRETEGE
zKv3.1 FWWAVVSMTTVGYGDMYPVTTIGGRIVGS.LCAIAGVLTIALEP.PVIVSN.FNYFYBRETEGE
zKv2.1 FWWAVVSMTTVGYGDMYPVTTIGGRIVGS.LCAIAGVLTIALEP.PVIVSN.FNYFYBRETEGE
hKv4.2 FWWAVVSMTTVGYGDMYPVTTIGGRIVGS.LCAIAGVLTIALEP.PVIVSN.FNYFYBRETEGE

(57) Abstract: The subject invention includes mutant voltage-gated ion channels that are open over a wide range of potential differences across membranes. The present invention also includes methods of use of such mutant voltage-gated ion channels in cells with highly negative potential differences across their membranes. One preferred mutant voltage-gated ion channel is a channel with a mutation at the residue homologous to P513 in Kv1.5 and at least one mutation at one of the residues homologous to R400, R403, and R409 in Kv1.5.

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